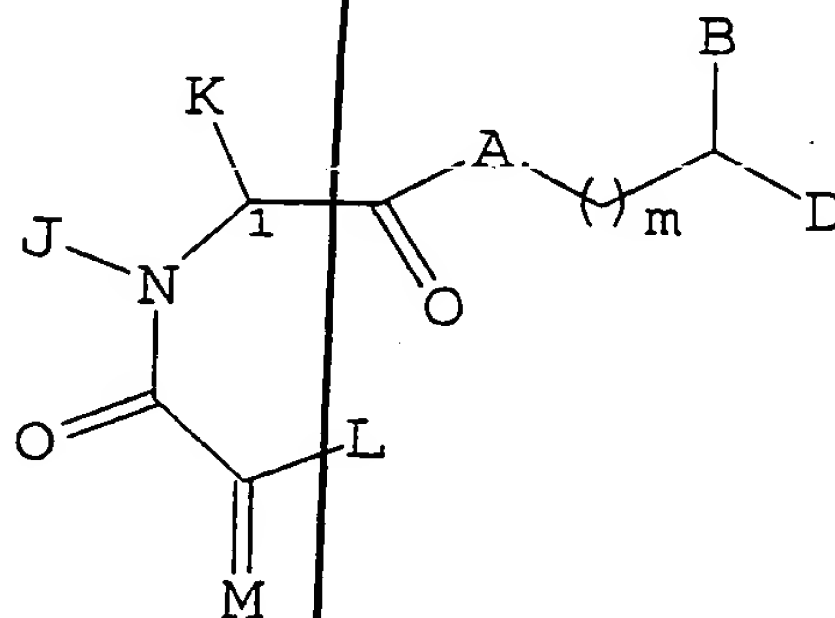


## WE CLAIM:

1. A method for treating alopecia or promoting hair growth in an animal, which comprises administering to said animal an effective amount of a pipecolic acid derivative of formula I

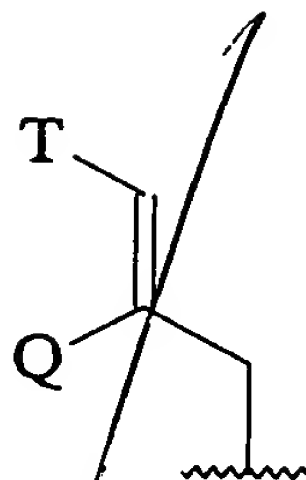


I

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A is  $\text{CH}_2$ , O, NH, or N-( $\text{C}_1$ - $\text{C}_4$  alkyl);

B and D are independently Ar,  $\text{C}_5$ - $\text{C}_7$  cycloalkyl substituted  $\text{C}_1$ - $\text{C}_6$  straight or branched chain alkyl or  $\text{C}_2$ - $\text{C}_6$  straight or branched chain alkenyl,  $\text{C}_5$ - $\text{C}_7$  cycloalkenyl substituted  $\text{C}_1$ - $\text{C}_6$  straight or branched chain alkyl or  $\text{C}_2$ - $\text{C}_6$  straight or branched chain alkenyl, or Ar substituted  $\text{C}_1$ - $\text{C}_6$  straight or branched chain alkyl or  $\text{C}_2$ - $\text{C}_6$  straight or branched chain alkenyl, wherein in each case, one or two carbon atom(s) of said alkyl or alkenyl may be substituted with one or two heteroatom(s) independently selected from the group consisting of oxygen, sulfur, SO, and  $\text{SO}_2$  in chemically reasonable substitution patterns, or



5

wherein Q is hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl; and

10

T is Ar or C<sub>5</sub>-C<sub>7</sub> cycloalkyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C<sub>1</sub>-C<sub>4</sub> alkyl), O-(C<sub>2</sub>-C<sub>4</sub> alkenyl), and carbonyl;

15

Ar is selected from the group consisting of 1-naphthyl, 2-naphthyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl, monocyclic and bicyclic heterocyclic ring systems with individual ring sizes being 5 or 6 which contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar contains 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl), O-benzyl, O-phenyl, amino,

25

1,2-methylenedioxy, carbonyl, and phenyl;

L is either hydrogen or U; M is either oxygen or CH-U, provided that if L is hydrogen, then M is CH-U, or if M is oxygen then L is U;

5 U is hydrogen, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl), C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl substituted with C<sub>1</sub>-C<sub>4</sub> straight or  
10 branched chain alkyl or C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl, (C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>2</sub>-C<sub>4</sub> alkenyl)-Ar, or Ar;

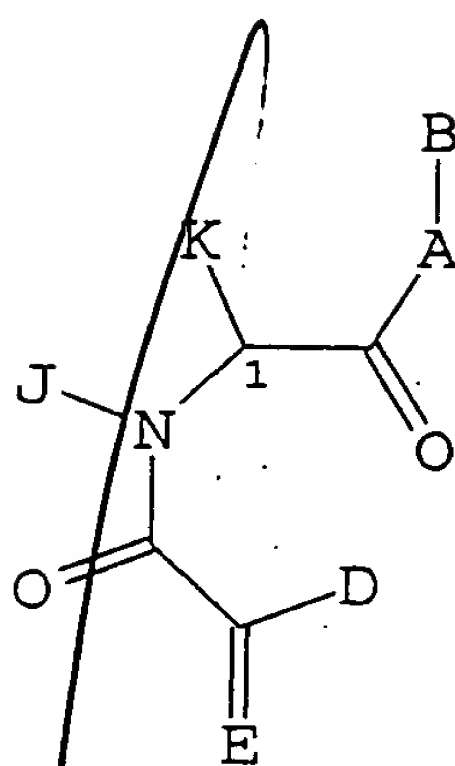
J is hydrogen, C<sub>1</sub> or C<sub>2</sub> alkyl, or benzyl; K is C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl, benzyl or cyclohexylmethyl; or J and K are taken together to  
15 form a 5-7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO<sub>2</sub>;

n is 0-3; and

said pipecolic acid derivative has an affinity for FKBP-type immunophilins.

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2. A method for treating alopecia or promoting hair growth in an animal, which comprises administering to said animal an effective amount of a pipecolic acid derivative of formula II

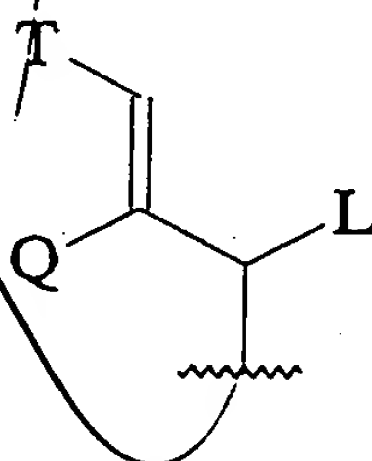


II

or a pharmaceutically acceptable salt, ester, or  
solvate thereof, wherein:

A is O, NH, or N-(C<sub>1</sub>-C<sub>4</sub> alkyl);

B is hydrogen, CHL-Ar, C<sub>1</sub>-C<sub>6</sub> straight or branched  
chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl,  
C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, Ar substituted C<sub>1</sub>-  
C<sub>6</sub> alkyl or C<sub>2</sub>-C<sub>6</sub> alkenyl, or



wherein L and Q are independently  
hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched chain  
alkyl, or C<sub>2</sub>-C<sub>6</sub> straight or branched chain  
alkenyl; and

T is Ar or C<sub>5</sub>-C<sub>7</sub> cyclohexyl substituted  
at positions 3 and 4 with substituents  
independently selected from the group  
consisting of hydrogen, hydroxy, O-(C<sub>1</sub>-C<sub>4</sub>

alkyl), O-(C<sub>2</sub>-C<sub>4</sub> alkenyl), and carbonyl;

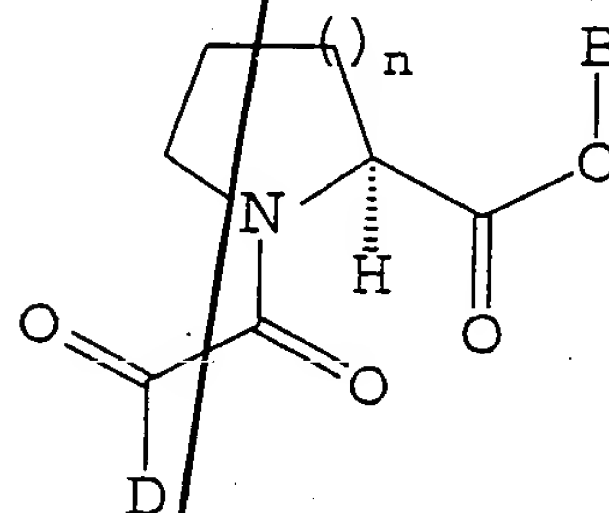
Ar is selected from the group consisting of 1-naphthyl, 2-naphthyl, 2-furyl, 3-furyl, 2-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl having 1-3  
 5 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain  
 10 alkenyl), O-benzyl, O-phenyl, amino, and phenyl.

D is hydrogen or U; E is oxygen or CH-U, provided that if D is hydrogen, then E is CH-U, or if E is oxygen, then D is U;

U is hydrogen, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain  
 15 alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl), C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, C<sub>5</sub>-C<sub>7</sub>-cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl substituted with C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>4</sub> straight or branched  
 20 chain alkenyl, 2-indolyl, 3-indolyl, (C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>2</sub>-C<sub>4</sub> alkenyl)-Ar, or Ar;

J is hydrogen, C<sub>1</sub> or C<sub>2</sub> alkyl, or benzyl; K is C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl, benzyl or cyclohexylethyl; or J and K are taken together to form  
 25 a 5-7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO<sub>2</sub>.

3. A method for treating alopecia or promoting hair growth in an animal, which comprises administering to said animal an effective amount of a pipecolic acid derivative of formula III



III

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

n is 2;

D is phenyl, methoxy, 2-furyl, or 3,4,5-trimethoxyphenyl; and

B is benzyl, 3-phenylpropyl, 4-(4-methoxyphenyl)butyl, 4-phenylbutyl, phenethyl, 3-cyclohexylpropyl, 4-cyclohexylbutyl, 3-cyclopentylpropyl, 4-cyclohexylbutyl, 3-phenoxybenzyl, 3-(3-indolyl)propyl, or 4-(4-methoxyphenyl)butyl;

provided that

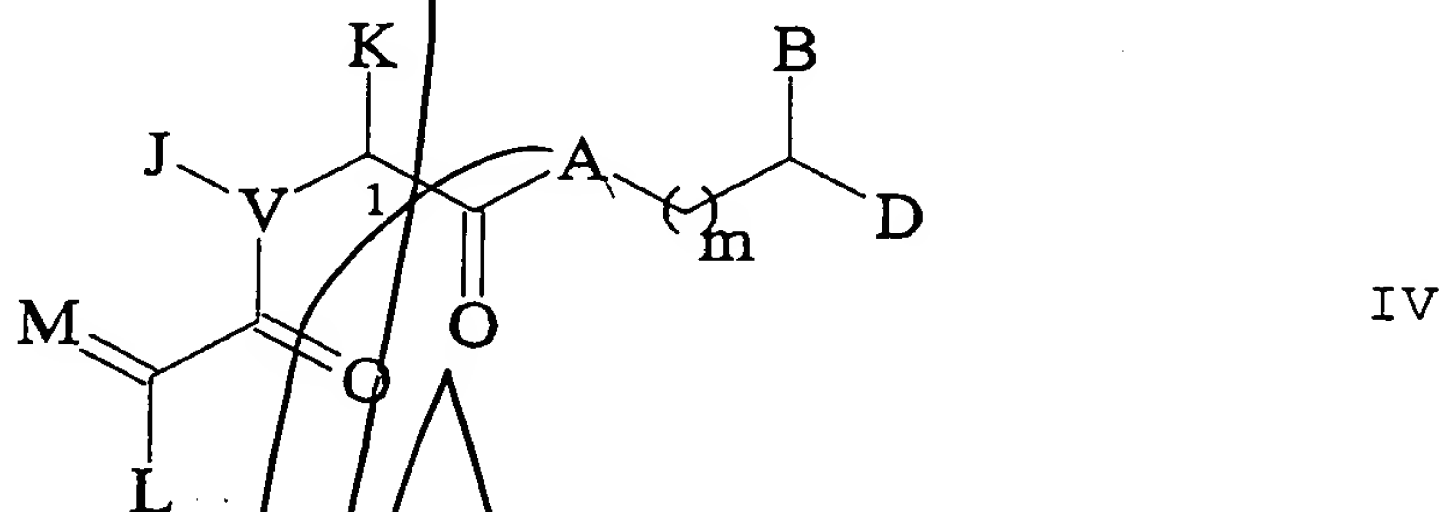
when D is phenyl, then B is benzyl, 3-phenylpropyl, 4-(4-methoxyphenyl)butyl, 4-phenylbutyl, phenethyl, or 4-cyclohexylbutyl;

when D is methoxy, then B is benzyl, 4-cyclohexylbutyl, 3-cyclohexylpropyl, or 3-cyclopentylpropyl;

when D is 2-furyl, then B is benzyl; and

when D is 3,4,5-trimethoxyphenyl, then B is  
4-cyclohexylbutyl, 3-phenoxybenzyl, 4-  
phenylbutyl, 3-(3-indolyl)propyl, or 4-(4-  
methoxyphenyl)butyl.

4. A method for treating alopecia or promoting  
hair growth in an animal, which comprises  
administering to said animal an effective amount of a  
pipecolic acid derivative of formula IV



or a pharmaceutically acceptable salt, ester, or  
solvate thereof, wherein:

V is C, N, or S;

J and K, taken together with V and the carbon  
atom to which they are respectively attached, form a  
5-7 membered saturated or unsaturated heterocyclic  
ring containing, in addition to V, one or more  
heteroatom(s) selected from the group consisting of O,  
S, SO, SO<sub>2</sub>, N, NH, and NR;

R is either C<sub>1</sub>-C<sub>9</sub> straight or branched chain  
alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>3</sub>-C<sub>9</sub>

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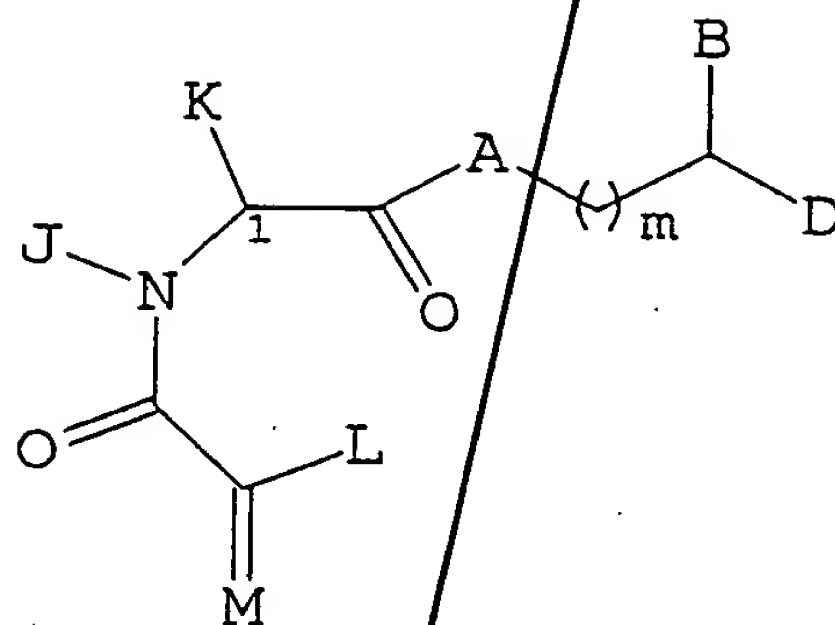
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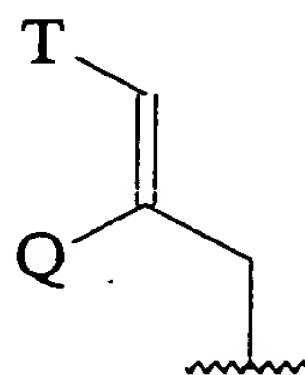


I

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A is  $\text{CH}_2$ , O, NH, or N-( $\text{C}_1$ - $\text{C}_4$  alkyl);

B and D are independently Ar,  $\text{C}_5$ - $\text{C}_7$  cycloalkyl substituted  $\text{C}_1$ - $\text{C}_6$  straight or branched chain alkyl or  $\text{C}_2$ - $\text{C}_6$  straight or branched chain alkenyl,  $\text{C}_5$ - $\text{C}_7$  cycloalkenyl substituted  $\text{C}_1$ - $\text{C}_6$  straight or branched chain alkyl or  $\text{C}_2$ - $\text{C}_6$  straight or branched chain alkenyl, or Ar substituted  $\text{C}_1$ - $\text{C}_6$  straight or branched chain alkyl or  $\text{C}_2$ - $\text{C}_6$  straight or branched chain alkenyl, wherein in each case, one or two carbon atom(s) of said alkyl or alkenyl may be substituted with one or two heteroatom(s) independently selected from the group consisting of oxygen, sulfur, SO, and  $\text{SO}_2$  in chemically reasonable substitution patterns, or



wherein Q is hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl; and

T is Ar or C<sub>5</sub>-C<sub>7</sub> cycloalkyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C<sub>1</sub>-C<sub>4</sub> alkyl), O-(C<sub>2</sub>-C<sub>4</sub> alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-naphthyl, 2-naphthyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl, monocyclic and bicyclic heterocyclic ring systems with individual ring sizes being 5 or 6 which contain in either or both rings a total of 1-4 heteroatoms independently selected from oxygen, nitrogen and sulfur; wherein Ar contains 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, hydroxymethyl, nitro, CF<sub>3</sub>, trifluoromethoxy, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl), O-benzyl, O-phenyl, amino, 1,2-methylenedioxy, carbonyl, and phenyl;

L is either hydrogen or U; M is either oxygen or CH-U, provided that if L is hydrogen, then M is CH-U, or if M is oxygen then L is U;

U is hydrogen, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl),

5 C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl substituted with C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl, (C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>2</sub>-C<sub>4</sub> alkenyl)-Ar, or Ar;

J is hydrogen, C<sub>1</sub> or C<sub>2</sub> alkyl, or benzyl; K is C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl, benzyl or cyclohexylmethyl; or J and K are taken together to form a 5-7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO<sub>2</sub>;

n is 0-3; and

said pipecolic acid derivative has an affinity for FKBP-type immunophilins; and

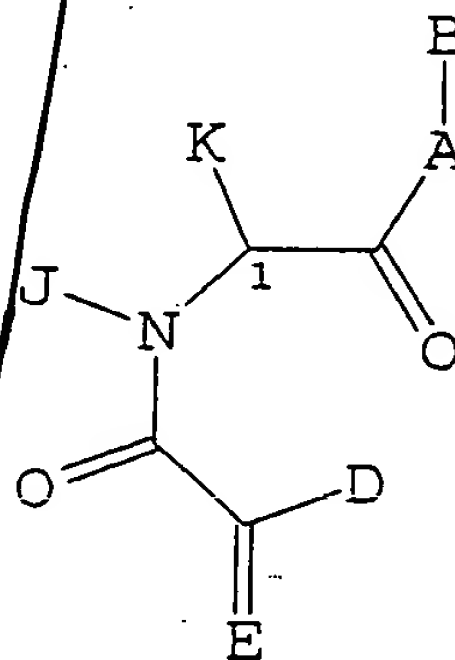
(ii) a pharmaceutically acceptable carrier.

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6. A pharmaceutical composition which comprises:

(i) an effective amount of a pipecolic acid derivative for treating alopecia or promoting hair growth in an animal, wherein the pipecolic acid derivative is a compound of formula II

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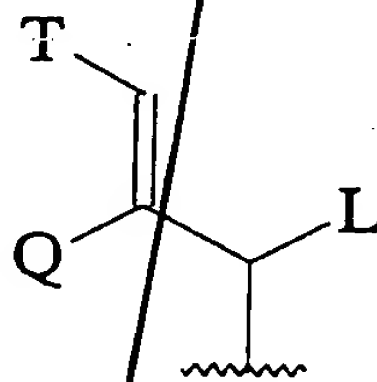


II

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

A is O, NH, or N-(C<sub>1</sub>-C<sub>4</sub> alkyl);

B is hydrogen, CHL-Ar, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, C<sub>5</sub>-C<sub>7</sub> cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl, Ar substituted C<sub>1</sub>-C<sub>6</sub> alkyl or C<sub>2</sub>-C<sub>6</sub> alkenyl, or



wherein L and Q are independently hydrogen, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, or C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl; and

T is Ar or C<sub>5</sub>-C<sub>7</sub> cyclohexyl substituted at positions 3 and 4 with substituents independently selected from the group consisting of hydrogen, hydroxy, O-(C<sub>1</sub>-C<sub>4</sub> alkyl), O-(C<sub>2</sub>-C<sub>6</sub> alkenyl), and carbonyl;

Ar is selected from the group consisting of 1-naphthyl, 2-naphthyl, 2-furyl, 3-furyl, 2-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl having 1-3 substituent(s) independently selected from the group consisting of hydrogen, halo, hydroxy, nitro, CF<sub>3</sub>, C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched

chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl), O-benzyl, O-phenyl, amino, and phenyl.

D is hydrogen or U; E is oxygen or CH-U, provided that if D is hydrogen, then E is CH-U, or if E is oxygen, then D is U;

U is hydrogen, O-(C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl), O-(C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl), C<sub>1</sub>-C<sub>6</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>6</sub> straight or branched chain alkenyl, C<sub>5</sub>-C<sub>7</sub>-cycloalkyl, C<sub>5</sub>-C<sub>7</sub> cycloalkenyl substituted with C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl or C<sub>2</sub>-C<sub>4</sub> straight or branched chain alkenyl, 2-indolyl, 3-indolyl, (C<sub>1</sub>-C<sub>4</sub> alkyl or C<sub>2</sub>-C<sub>4</sub> alkenyl)-Ar, or Ar;

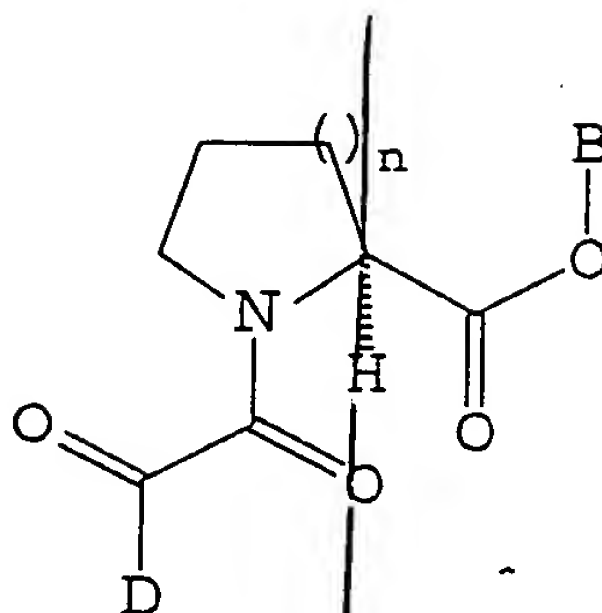
J is hydrogen, C<sub>1</sub> or C<sub>2</sub> alkyl, or benzyl; K is C<sub>1</sub>-C<sub>4</sub> straight or branched chain alkyl, benzyl or cyclohexylethyl; or J and K are taken together to form a 5-7 membered heterocyclic ring which is substituted with oxygen, sulfur, SO, or SO<sub>2</sub>; and

(ii) a pharmaceutically acceptable carrier.

7. A pharmaceutical composition which comprises:

(i) an effective amount of a pipecolic acid derivative for treating alopecia or promoting hair growth in an animal, wherein the pipecolic acid derivative is a compound of formula III

1. *Chlorophyll a* (Chl a) content was determined using a spectrophotometer (Shimadzu UV-1601) at 663 nm. The concentration of Chl a was calculated using the following equation:  $\text{Chl a (mg/L)} = 12.7 \times \text{OD}_{663}$ .



III

or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

```
10      n is 2;
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D is phenyl, methoxy, 2-furyl, or 3,4,5-trimethoxyphenyl; and

B is benzyl, 3-phenylpropyl, 4-(4-methoxyphenyl)butyl, 4-phenylbutyl, phenethyl, 3-cyclohexylpropyl, 4-cyclohexylbutyl, 3-cyclopentylpropyl, 4-cyclohexylbutyl, 3-phenoxybenzyl, 3-(3-indolyl)propyl, or 4-(4-methoxyphenyl)butyl;

provided that

when D is phenyl, then B is benzyl, 3-phenylpropyl, 4-(4-methoxyphenyl)butyl, 4-phenylbutyl, phenethyl, or 4-cyclohexylbutyl;

when D is methoxy, then B is benzyl, 4-cyclohexylbutyl, 3-cyclohexylpropyl, or 3-cyclopentylpropyl;

25                    when D is 2-furyl, then B is benzyl; and

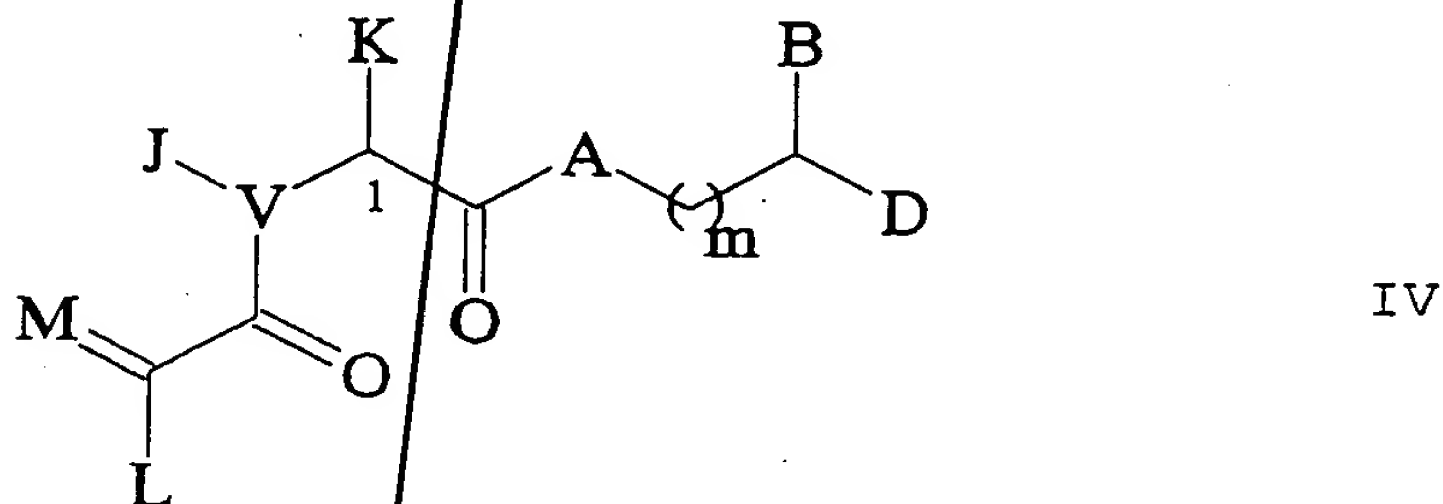
when D is 3,4,5-trimethoxyphenyl, then B is 4-cyclohexylbutyl, 3-phenoxybenzyl, 4-phenylbutyl, 3-(3-indolyl)propyl, or 4-(4-

methoxyphenyl)butyl; and

(ii) a pharmaceutically acceptable carrier.

8. A pharmaceutical composition which comprises:

(i) an effective amount of a pipecolic acid derivative for treating alopecia or promoting hair growth in an animal, wherein the pipecolic acid derivative is a compound of formula formula IV



or a pharmaceutically acceptable salt, ester, or solvate thereof, wherein:

V is C, N, or S;

J and K, taken together with V and the carbon atom to which they are respectively attached, form a 5-7 membered saturated or unsaturated heterocyclic ring containing, in addition to V, one or more heteroatom(s) selected from the group consisting of O, S, SO, SO<sub>2</sub>, N, NH, and NR;

R is either C<sub>1</sub>-C<sub>9</sub> straight or branched chain alkyl, C<sub>2</sub>-C<sub>9</sub> straight or branched chain alkenyl, C<sub>3</sub>-C<sub>9</sub> cycloalkyl, C<sub>3</sub>-C<sub>9</sub> cycloalkenyl, or Ar<sub>1</sub>, wherein R is

[illegible]

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15

(ii) a pharmaceutically acceptable carrier.